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| 10/511,148 | 12/02/2004 | Alan Michael Sawyer | 2004_1542A | 9045 |

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| EXAMINER | |
|---|---|
| SANG, HONG | |
| ART UNIT | PAPER NUMBER |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/511,148 | SAWYER ET AL. | |
| | Examiner | Art Unit | |
| | HONG SANG | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2,4-13,16,17 and 20-31* is/are pending in the application.

4a) Of the above claim(s) *16,17,20-26,29 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-13,27,28 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/14/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

**RE: Sawyer et al.**

***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/13/2008 has been entered.

2. Applicant's species election of purified proteinaceous substances (including purified proteinaceous substances linked to a carrier, and fragments thereof) and peptides in the reply filed on 11/19/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 1, 2, 4-13, 16, 17 and 20-31 are pending. New claims 28-31 have been added. Claims 3, 14-15 and 18-19 have been cancelled. Claims 16, 17 and 20-26 have been withdrawn from consideration. Claims 1 and 27 have been amended. Due to species election, claims 29 and 31 are withdrawn from further consideration as being drawn to non-elected inventions.

4. Claims 1, 2, 4-13, 27, 28 and 30 are under examination. Due to species election, claims are examined to the extent that the purified candidate antigens are purified proteinaceous substances, and the purified proteinaceous substances are peptides.

***Rejections Withdrawn***

5. The rejection of claims 1, 2, 4-13 and 27 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Mather et al (WO/2000/037503; Publication Date: 06/29/2000) in view of Kucherlapati et al (US Patent 6150584; Date Issued: 11/21/2000) and van de Winkel et al (PGPUB 20030138421; Publication Date: 07/24/2003) and Rava et al (US Patent 6720149; Date Filed 05/28/2002, Claims priority to 10/10/1999) and Kessler et al (PGPUB 20030044849; Date Filed:08/21/2002, Claims priority to 10/22/2001) is withdrawn in view of applicant's amendment to the claims.

***New Grounds of Objection and Rejection***

***Claim Objections***

6. Claim 7 is objected to for reciting "wherein the antibody-producing cells are B cells, T cell or stem cells" because only B cells are known in the art to produce antibody.

7. Claim 27 is objected to for reciting the phrase "a single suspension of antibody-producing cells". The meaning of the phrase is unclear. Does it mean "a single cell suspension of antibody-producing cells"?

Appropriate correction is required.

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 2, 4-13, 27, 28 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen (CN 1274085A, Pub. Date: 11/22/2000, see the English translation submitted with IDS on 5/3/2007), in view of Rava et al (US Patent 6,720,149; Date of Patent: 4/13/2004, earliest effective filing date: 6/7/1994), Klessing et al. (US 5,989,846, Date of Patent: 11/23/1999), Poethke et al. (Biol. Chem., 1997, 378: 997-1004), Hu (US 2002/0048823A1, Pub. Date: 4/25/2002, earliest effective filing date: 8/11/2000), and Sanderson et al. (US, 6,821,517B1, Date of Patent 11/23/2004, earliest effective filing date: 10/18/1996).

Chen discloses a method for large scale screening monoclonal antibodies comprising the steps: immunizing BALB/c mice with homogenized tissue; fusing spleen cells and myelomas of BALB/c; separating individual hybridomas with a flow-type cell meter and raising a culture; preparing a protein chip used for identifying the antibodies produced while at the same time establishing a hybridoma bank; preparing a protein chip for screening use and using specific antigens and polyclonal antibodies to screen for the corresponding monoclonal antibodies (see the English translation, abstract). With respect to the protein chip, Chen discloses that a large quantity of specific antigens or antibodies are fixed in sequence on a carrier, which can be a cellulose film, a nylon film or a glass plate, to form an array utilizing the antigen-antibody affinity reaction to detect corresponding antibody or antigen (see the English translation, claim 1). Chen discloses a method of using the protein chip for screening monoclonal antibodies,

characterized by using specific antigens and polyclonal antibodies to screen for the corresponding monoclonal antibodies, the method comprising: (1) adding antigen to the protein chip and incubate for 30-60 min, (2) washing 3-5 times, (3) adding FITC labeled polyclonal antibodies giving immunity to specific antigens to the protein chip, and incubate for 30-60 mins, (4) observing the protein chip under the fluorescence microscope, selecting the fluorescing colored dots and extracting the corresponding hybridomas from the hybridoma bank, culturing and identifying the screened monoclonal antibodies, (5) substituting another antigen and its fluorescent labeled polyclonal antibody and repeating the steps (1)-(4) to screen out another monoclonal antibody (see the English translation, claim 5). Chen discloses the classic screening methods for specific monoclonal antibodies, including the use of an antigen enveloped carrier, wherein the supernatant fluid from the monoclonal hybridoma culture to be measure is added, if the supernatant fluid contains the corresponding monoclonal antibody, it binds with the enveloping antigen (see the English translation, specification, page 1, last paragraph). Chen discloses that the shortcoming of the classic screening methods for specific antibodies is that only one antibody from the numerous clones can be screened out, and by using a protein chip it is possible to detect a large quantity of antigen-antibody binding reactions rapidly (see the English translation, specification, page 2, paragraph 1). Chen teaches that if homogenized tissue is used to immunize mice, and the antibodies secreted by the cloned hybridomas are fixed on a carrier, it is possible to screen for different antigen monoclonal antibody hybridoma strains by using different antigens and their polyclonal antibodies (see the English translation,

specification, page 2, paragraph 2). Chen discloses that the mice were immunized with liver homogenate, which were further immunized at intervals of 2-4 weeks, and after 4 weeks an immunization booster was give intravenously (see the English translation, specification, page 8).

Chen does not teach screening antibodies using a protein chip on which the purified candidate antigens are displayed. Chen does not disclose immunizing animals using purified proteinaceous substance such as peptides, wherein between two and fifty different purified candidate antigens are introduced into each animal and between 0.001 and 1000 micrograms of each antigen is introduced into each animal. Chen does not teach isotyping the monoclonal antibodies using isotype specific anti-immunoglobulin antibodies, wherein each anti-immunoglobulin antibody having different isotype specificity has a different label. However, these deficiencies are made up for in the teachings of Rava, Klessing, Poethke, Hu and Sanderson.

Rava et al teach methods for concurrently processing multiple biological chip assays by providing a biological chip plate comprising a plurality of test wells, each test well having a biological chip having a molecular probe array; introducing samples into the test wells; subjecting the biological chip plate to manipulation by a fluid handling device that automatically performs steps to carry out reactions between target molecules in the samples and probes; and subjecting the biological chip plate to a biological chip plate reader that interrogates the probe arrays to detect any reactions between target molecules and probes (abstract, in particular). Rava et al teach that a probe can be selected from proteins of interest and the targets can be selected from

monoclonal antibodies and the antisera reactive with specific antigenic determinants (detailed description, paragraph 3; in particular).

Klessing et al. teach immunizing mice with a purified protein mixture comprising two prevalent proteins and a number of other less abundant proteins (see column 26, lines 40-43). The mice was first immunized with 50 mg of proteins, and then injected two more times (two and five weeks later), each time with an addition 50 micrograms of proteins (column 27, Example 12). Klessing et al. teach that the B cells produced antibodies to each of the various proteins in the mixture (see column 26, lines 43-49). Klessing et al. disclose that the progeny of each independent B cell fused with a myeloma cell were grown separately, and the monoclonal antibody was individually tested to determine if the antibody recognized any one of the proteins in the partially purified protein mixture (see column 26, lines 54-65).

Poethke et al. teach immunizing mice with a mixture of eight synthetic ChAT-peptides coupled to KLH (20 microgram each), wherein the peptides were deduced from the primary structures of porcine and human ChAT (see abstract and page 1003, paragraph 1). Poethke et al. teach a method of screening of hybridoma supernatants using ELISA, wherein a mixture of 8 peptides was employed for coating the microtiter plate and the immobilized peptides were challenged with the hybridoma supernatants (see page 1003, paragraphs 2 and 3). Poethke et al. disclose that for epitope analysis the wells of microtiter plates were coated with synthetic peptides and subsequently incubated with hybridoma supernatants (see page 1004, column 1).

Hu discloses that a plurality of monoclonal antibodies can be produced by immunizing one or more animals with randomized peptides or natural antigens (see paragraph [0010]). Hu discloses that a library of peptides may be synthesized to generate antibodies (see paragraph [0024]).

Sanderson et al. teach antibody isotyping by ELISA using 96 well microtiter plates coated with appropriate peptide and rabbit anti-mouse IgA, IgG1, IgG2a, IgG2b, IgG3 and IgM (see column 18, lines 44-63). Although Sanderson et al. do not disclose that rabbit anti-mouse IgA, IgG1, IgG2a, IgG2b, IgG3 and IgM each has a different label, using different labels in the ELISA or microarray assay was known in the art as shown by Ho. Ho et al. teach detecting and identifying target antigens using antibody microarray wherein the target antigens have same tag or label or different tags or labels (see paragraph [0030].

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Chen to immunize the animals with purified proteins (or peptides) for the production of a population of monoclonal antibodies that bind the purified proteins (or peptides) and further use the protein chip coated with the purified proteins (or peptides) instead of the monoclonal antibodies for large scale screening of monoclonal antibodies in view of the teachings of Rava, Klessing, Poethke, and Hu. One of ordinary skill in the art would have been motivated to do so because purified proteins (or peptides) were used in the prior art to produce monoclonal antibodies that bind them, as well as identify the produced monoclonal antibodies, as shown by the teachings of Klessing, Poethke and Hu,. With

respect to the protein chip, Chen discloses that a large quantity of specific antigens or antibodies are fixed in sequence on a carrier to form an array utilizing the antigen-antibody affinity reaction to detect corresponding antibody or antigen (see the English translation, claim 1). Therefore, for screening monoclonal antibodies, a protein chip coated with known antigens is an alternative of the protein chip coated with antibodies taught by Chen. This is further evidenced by Rava et al., who teach a method of screening monoclonal antibodies using a microarray coated with antigens. The claims would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. One of ordinary skill in the art would have had a reasonable expectation of success to modify the method of Chen because immunizing animals with purified proteins (or peptides) for the production of a population of antibodies were known in the art as shown by Klessing, Poethke, and Ho, and the method of screening monoclonal antibodies using microarray coated with corresponding antigens was taught by Rava. In addition, it would have been *prima facie* obvious to one of ordinary skill in the art and one of ordinary skill in the art would have been motivated to determine the isotypes of the monoclonal antibodies for the purpose of further characterization of the monoclonal antibodies. One of ordinary skill in the art would have reasonable expectation of success to do so because the method of determination of an antibody isotype was well known in the art as shown by the teachings of Sanderson.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

***Conclusion***

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to HONG SANG whose telephone number is (571)272-8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Hong Sang/
Examiner, Art Unit 1643
1/9/2008